familial idiopathic basal ganglia calcification

Familial idiopathic basal ganglia calcification (FIBGC, formerly known as Fahr disease) is a condition characterized by abnormal deposits of calcium (calcification) in the brain. These calcium deposits typically occur in the basal ganglia, which are structures deep within the brain that help start and control movement; however, other brain regions can also be affected.

The signs and symptoms of FIBGC include movement disorders and psychiatric or behavioral difficulties. These problems begin in adulthood, usually in a person's thirties. The movement difficulties experienced by people with FIBGC include involuntary tensing of various muscles (dystonia), problems coordinating movements (ataxia), and uncontrollable movements of the limbs (choreoathetosis). Affected individuals often have seizures as well. The psychiatric and behavioral problems include difficulty concentrating, memory loss, changes in personality, a distorted view of reality (psychosis), and decline in intellectual function (dementia). An estimated 20 to 30 percent of people with FIBGC have one of these psychiatric disorders.

The severity of this condition varies among affected individuals; some people have no symptoms related to the brain calcification, whereas other people have significant movement and psychiatric problems.

Frequency

FIBGC is thought to be a rare disorder; about 60 affected families have been described in the medical literature. However, because brain imaging tests are needed to recognize the calcium deposits, this condition is believed to be underdiagnosed.

Genetic Changes

Mutations in the *SLC20A2* gene cause nearly half of all cases of FIBGC. A small percentage of cases are caused by mutations in the *PDGFRB* gene. Other cases of FIBGC appear to be associated with changes in chromosomes 2, 7, 9, and 14, although specific genes have yet to be identified. These findings suggest that multiple genes are involved in this condition.

The *SLC20A2* gene provides instructions for making a protein called sodium-dependent phosphate transporter 2 (PiT-2). This protein plays a major role in regulating phosphate levels within the body (phosphate homeostasis) by transporting phosphate across cell membranes. The *SLC20A2* gene mutations that cause FIBGC lead to the production of a PiT-2 protein that cannot effectively transport phosphate into cells. As a result, phosphate levels in the bloodstream rise. In the brain, the excess phosphate combines with calcium and forms deposits.

The *PDGFRB* gene provides instructions for making a protein that plays a role in turning on (activating) signaling pathways that control many cell processes. It is unclear how *PDGFRB* gene mutations cause FIBGC. Mutations may alter signaling within cells that line blood vessels in the brain, causing them to take in excess calcium, and leading to calcification of the lining of these blood vessels. Alternatively, changes in the PDGFRB protein could alter phosphate transport signaling pathways, causing an increase in phosphate levels and the formation of calcium deposits.

Researchers suggest that calcium deposits lead to the characteristic features of FIBGC by interrupting signaling pathways in various parts of the brain. Calcium deposits may disrupt the pathways that connect the basal ganglia to other areas of the brain, particularly the frontal lobes. These areas at the front of the brain are involved in reasoning, planning, judgment, and problem-solving. The regions of the brain that regulate social behavior, mood, and motivation may also be affected.

Research has shown that people with significant calcification tend to have more signs and symptoms of FIBGC than people with little or no calcification. However, this association does not apply to all people with FIBGC.

Inheritance Pattern

FIBGC is inherited in an autosomal dominant pattern. Autosomal dominant inheritance means one copy of an altered *SLC20A2* or *PDGFRB* gene in each cell is sufficient to cause the disorder. This condition appears to follow an autosomal dominant pattern of inheritance when the genetic cause is not known. In most cases, an affected person has one parent with the condition.

Other Names for This Condition

- bilateral striopallidodentate calcinosis
- cerebrovascular ferrocalcinosis
- FIBGC
- striopallidodentate calcinosis

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Basal ganglia calcification, idiopathic, 2
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1847731/
- Genetic Testing Registry: Basal ganglia calcification, idiopathic, 4
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3554321/
- Genetic Testing Registry: Idiopathic basal ganglia calcification 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0393590/

Other Diagnosis and Management Resources

- Dystonia Medical Research Foundation: Treatments
  https://www.dystonia-foundation.org/living-with-dystonia/treatments
- GeneReview: Primary Familial Brain Calcification
  https://www.ncbi.nlm.nih.gov/books/NBK1421

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Basal Ganglia Dysfunction
  https://medlineplus.gov/ency/article/001069.htm
- Encyclopedia: Brain
  https://medlineplus.gov/ency/imagepages/1074.htm
- Encyclopedia: Calcification
  https://medlineplus.gov/ency/article/002321.htm
- Encyclopedia: Cranial Calcification (image)
  https://medlineplus.gov/ency/imagepages/9228.htm
- Health Topic: Brain Diseases
  https://medlineplus.gov/braindiseases.html
- Health Topic: Seizures
  https://medlineplus.gov/seizures.html

Genetic and Rare Diseases Information Center

- Primary Familial Brain Calcification
  https://rarediseases.info.nih.gov/diseases/6406/primary-familial-brain-calcification

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Fahr's Syndrome Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Fahrs-Syndrome-Information-Page

Educational Resources

- Boston Children's Hospital: Seizures and Epilepsy
  http://www.childrenshospital.org/conditions-and-treatments/conditions/seizures
- Cleveland Clinic: Dementia
  http://my.clevelandclinic.org/health/articles/types-of-dementia
- Cleveland Clinic: Epilepsy: Frequently Asked Questions
  http://my.clevelandclinic.org/health/articles/epilepsy-frequently-asked-questions
- Disease InfoSearch: Familial idiopathic basal ganglia calcification
  http://www.diseaseinfosearch.org/Familial+idiopathic+basal+ganglia+calcification/9573
- Kennedy Krieger Institute: Epilepsy (Seizure Disorder)
  https://www.kennedykrieger.org/patient-care/diagnoses-disorders/epilepsy-seizure-disorder
- Kennedy Krieger Institute: Movement Disorders
  https://www.kennedykrieger.org/patient-care/diagnoses-disorders/movement-disorders
- Merck Manual Home Edition for Patients and Caregivers: Dystonia
  http://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/movement-disorders/dystonia
- Orphanet: Bilateral striopallidodentate calcinosis
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1980

Patient Support and Advocacy Resources

- CLIMB: Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk/
- Dystonia Medical Research Foundation
  https://www.dystonia-foundation.org/
- Family Caregiver Alliance
  https://www.caregiver.org/
- National Ataxia Foundation
  http://www.ataxia.org/

- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/primary-familial-brain-calcification/
- University of Kansas Medical Center Resource List: Psychiatric Conditions/ Behavior Genetics
  http://www.kumc.edu/gec/support/psych.html

GeneReviews

- Primary Familial Brain Calcification
  https://www.ncbi.nlm.nih.gov/books/NBK1421

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28familial+idiopathic+basal+ganglia+calcification%5BTIAB%5D%29+OR+%28idiopathic+basal+ganglia+calcification%5BTIAB%5D%29+OR+%28fahr+disease%5BTIAB%5D%29+OR+%28fibgc%5BTIAB%5D%29+OR+%28fahr's+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- BASAL GANGLIA CALCIFICATION, IDIOPATHIC, 1
  http://omim.org/entry/213600
- BASAL GANGLIA CALCIFICATION, IDIOPATHIC, 2
  http://omim.org/entry/606656
- BASAL GANGLIA CALCIFICATION, IDIOPATHIC, 4
  http://omim.org/entry/615007

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Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/familial-idiopathic-basal-ganglia-calcification

Reviewed: February 2013
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
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